UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,428	03/19/2001	Magnus Hook	P06668US03/BAS	6490

881 7590 05/17/2006

STITES & HARBISON PLLC
1199 NORTH FAIRFAX STREET
SUITE 900
ALEXANDRIA, VA 22314

EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/810,428	HOOK ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7,13-22, 27-,29,30,33 and 34* is/are pending in the application.

4a) Of the above claim(s) *15-22,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7,13,14,23,29,30,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/10/06 has been entered.

Amendment/Status of Claims

2. The amendment filed on 2/10/06 has been entered.
Claims 2, 6, 8-12, 11, 24-26, 31 and 32 are canceled.
Claims 1, 13 and 23 have been amended.

Claims 1, 3-5, 7, 13, 14, 23, 29, 30 and 33-34 are under examination as an elected invention.

Claims 15-22 and 27-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention.

New Claim Rejections based on amendment

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 3-5, 7, 13, 14, 23, 29, 30 and 33-34 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated monoclonal antibody, 11 H11 which recognizes the central region of the collagen binding domain from the *S. aureus* CNA protein, said antibody cross-reacts to both *S. aureus and S. epidermidis*, said antibody inhibits adhesion of *S. aureus* to collagen and displaces *S. aureus* bound to collagen, a

diagnostic kit and a composition comprising said mAb does not reasonably provide enablement for an isolated cross-reactive monoclonal antibody which recognizes the binding region at amino acids 151-318 of the collagen binding domain from the *S. aureus* CNA protein Or an isolated monoclonal antibody that is cross reactive to both *S. aureus* and *S. epidermidis* which is generated against amino acids 151-318 of the collagen binding domain of the S. aureus CNA protein, and is capable of inhibiting adhesion of *S. aureus* to collagen and displacing *S. aureus* bound to collagen, a diagnostic kit and a pharmaceutical composition comprising said mAb. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims are drawn to an isolated cross-reactive monoclonal antibody which recognizes the binding region at amino acids 151-318 of the collagen binding domain from the *S. aureus* CNA protein, wherein said antibody is cross-reactive to both *S. aureus* and *S. epidermidis*, and wherein said antibody is capable of inhibiting adhesion of *S. aureus* to collagen and displacing *S. aureus* bound to collagen, a diagnostic kit and a pharmaceutical composition comprising said mAb.

The instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is making and screening monoclonal antibodies that bind to various epitopes (i.e., 20-25 amino acids) within 151-318 amino acid collagen binding domain. One of the monoclonal antibody 11 H11 cross-reacts to both *S. aureus and S. epidermidis*. The same antibody inhibits adhesion of *S. aureus* to collagen and displaces *S. aureus* bound to collagen (see specification on page 8-14 and 37-45). However, the specification fails to provide enablement for any other monoclonal antibody that has the same functional characteristics (see page 44 especially). Further, the prior art (for example: see APPENDIX A) provided by the applicant 2/10/06 also indicates that various MAbs recognized epitopes located throughout the CNA- (151-318) molecule. In all, two mAbs were mapped to the N-terminal quarter (2B1and 9F11), 15 (1F6, 283, 3D3, 5G4, 7C2, 7E2, 7G2, 8E6, 8H10, 9A4, 9G3, 9G7, I 1D5, 11H11, 161-19) mapped to the central region, and 5 mapped to the C-terminal end of CNA- (IH1, 3B12, 5D12, 5H1, I2H10). Thus, it is apparent that the epitopes recognized by CNA mAbs are distributed throughout the entire structure of CNA- (151-318). Some mAbs caused the detachment of staphylococcal cells that had adhered to the collagen substrate during a 1-h incubation before the addition of mAbs (Fig. 6B). mAb 9G7, which effectively released ^{125}I-collagen bound to the bacterial surface, also effectively detached pre-attached bacterial from a collagen substrate. mAb 11H11caused partial detachment, whereas 8E6 and 16H9, which were essentially inactive in the detachment assay, also had little or no effect, respectively, in the displacement assay. None of the mAbs shown to be useful for treating or preventing infection caused by *S. aureus and S. epidermidis*. Although the number of mAbs that were analyzed in all assays, it is unclear whether all these monoclonal antibodies could be used for identifying both Staphylococcal and Streptococcal bacterial antigens such that they can be used for treating or preventing infections caused by *S. aureus and S. epidermidis*. Thus, monoclonal antibodies that bind to amino acids 151-318 molecule must be considered highly

unpredictable because it is highly unlikely all monoclonal antibodies that bind to amino acids 151-318 can cross react to both *S. aureus and S. epidermidis*, inhibits adhesion of *S. aureus* to collagen and displacing *S. aureus* bound to collagen based on the evidence the art of record. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

5. If applicant amends the claims to recite the monoclonal antibody 11H11, applicant is advised to provide deposit information of the monoclonal antibodies as a required element because it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line / hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

NOTE THE CURRENT ATCC DEPOSITORY ADDRESS
American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209

Applicant is reminded that the following and should amend the specification accordingly. The current address of the ATCC is as follows:
American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Claim Rejections - 35 USC 102 maintained

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office actions.

6. The rejection of claims 1, 3-5, 7, 13, 14, 23, 29, 30 and 33-34 under 35 U.S.C. 102(e) as being anticipated by Hook et al 2001 U.S.Patent 6,288,214 is maintained as set forth in the previous office action.

The disclosed monoclonal antibodies to SEQ.ID.NO: 6 of the Patent bind to amino acids 30-531 of the full length CNA protein. Therefore, these antibodies bind to CNA 19 peptide of the present application that contains amino acids 151-318 of the full-length CNA protein and prevent *S.aureus* infection. The antibodies disclosed in the patent are monoclonal antibodies and are used as pharmaceutical composition to treat *S.aureus* infection (see abstract, figures 5-7 and columns 15-19). Further the prior art discloses antibodies that prevent *S.aureus* infection (i.e., antibody capable of displacing *S.aureus* to collagen, (see figures 7- 8) and other related bacterial colonies (column 4, lines 45-50). Therefore, the disclosed antibodies are cross-reactive to *S.epidermidis*. The prior art also discloses diagnostic kits comprising the antibodies (column 26). Since the Office does not have the facilities for examining and comparing applicants' product and method of use with the product and method of use of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430. The prior art anticipated the claimed invention.

7. The rejection of claims 1, 3-5, 7, 13, 14, 23, 29, 30 and 33-34 35 U.S.C. 102(b) as being anticipated by Hook et al WO97/43314 20 November 1997 (20.11.1997) is maintained as set forth in the previous office action.

Hook et al disclose the 19,000 M collagen-binding domain from Staphylococcus aureus, also known as CNA-19. The 19kD protein contains the 168 amino acid long segments, specifically amino acids 151-318 of the protein that has appreciable collagen binding activity (page 3). Hook et al., disclose the preparation of immunological compositions such as anti-collagen binding protein (CBP) antibodies for diagnostic and therapeutic methods for detection and treatment of infections caused by S. aureus s (page 16). The antibody compositions disclosed bind to altered proteins, specific to native collagen and synthetically mutated CBP with domain specific epitopes within the CBPs (page 16). The antibodies have been shown to inhibit collagen binding to CBP and *S.aureus* binding to extra cellular matrix by both in vitro and in vivo (page 26 and claims) assays. Hence the antibodies displace *S.aureus* bound to collagen. The antibodies are monoclonal (page 26 and claims) antibodies and interact with collagen binding domain of a staphylococcal cna gene product (claim 1). Therefore, the antibodies could cross react with other staphylococcal cna gene products such as *S.epidermidis*. The vaccine formulation are useful against streptococcal and staphylococcal infection (page 29). The therapeutic and diagnostic kits comprising CBP compositions include antibodies and labels (page 37-39). The administration of antibodies reactive with CBP to at-risk subjects will be effective for prophylaxis of and in the case of infected subjects for therapy of bacterial infections (page 17). Preferred animals to receive treatment include mammals and particularly humans (page 18). Also taught were immunoassays for detection in ELISA plates, dot blots and western analysis (page 20). Exemplary samples include clinical samples of blood and serum (page 21). Also taught are methods for inhibiting bacterial adhesion to collagen (page 22). Therefore, in the absence of evidence to the contrary the disclosed antibodies against CNA read on the claimed invention. Since the Office does not have the facilities for examining and comparing applicants' product and method of use with the product and method of use of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product

and the product of the prior art. See In re Best, 562 F.2d 1252, and 195 USPQ 430. The prior art anticipated the claimed invention.

Applicant states that the U.S.Patent 6,288,214 and WO97/43314 do not disclose or suggest the claimed invention because the monoclonal antibodies as claimed are epitope specific and gave an excellent results in achieving protection and it is extremely unlikely that monoclonal antibodies raised against greater region (amino-acid 30-531) would be able to recognize the specific epitope within a given region. The cross reactivity of the antibodies is unexpected. In addition, Applicant provided Appendix A, Visai et al, Journal of Biological Chemistry, 275 (51): 39837- 39845 (Dec. 2000) which discusses the experiments regarding the displacement ability of monoclonal antibodies to the CNA 151-318 region as supporting evidence.

The examiner reviewed the Appendix A, applicant's arguments with respect to the claimed invention. The appendix A indicates that monoclonal antibodies (i.e., mAb, 9G7, 11H11, 8E6 and 16H9 etc) recognized only 20-25 amino acid epitope in 151-318 CNA protein. Therefore, the mAb of evidence of record are different from that of the broadly claimed monoclonal antibodies. Further, the claimed isolated monoclonal antibody has not been distinguished (for example: structure or epitope) from that of antibodies to full length CNA. Therefore, in the absence of evidence, the disclosed antibodies have the same function.

The appendix A indicates that epitope recognized by mAbs are distributed throughout the entire structure of CNA 151-318 rather than recognizing the 161 amino acids of binding domain 151-318. However, the claimed antibody was not distinguished from the disclosed prior art antibodies, which inhibited the *S.aureus* infection by preventing the bacterial adhesion (i.e., collagen binding). Therefore, the disclosed antibody is the same as that of claimed antibody.

Additionally, as Applicants are aware that conformational epitope of the CNA protein and the monoclonal antibody that binds to such epitope is very important as shown in the evidence

provided by the applicant. Therefore, in the absence of evidence to the contrary, the prior art monoclonal antibodies that confer protection against *S.aureus* infection and inhibiting the collagen binding read on the claimed invention.

Remarks

8. No claims are allowed.

Conclusion

9. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600